Safe Drugs Save Lives

# NATIONAL DRUG AUTHORITY

# PHARMACOVIGILANCE BULLETIN

INSIDE THIS ISSUE



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# Editorial

Welcome to this edition of the Pharmacovigilance Bulletin. In this issue, we share dedicated channels for reporting adverse drug reactions due to Covid-19 medicines and as always encourage you to continue reporting all adverse events to all other medicines. There has been an almost 50% decrease in the number of reports received from 465 (January to March 2020) to 209 reports (April to June 2020). Whereas we appreciate the challenges of lockdown and curfew on movements and health facility volumes, we remind you to remain alert for any suspicious products and adverse drug events and report them promptly.

Haemovigilance is a fairly uncharted territory of pharmacovigilance and this issue discusses some cases of reactions to blood and blood products that we have received at National Drug Authority to raise awareness.

One of our roles at the National Pharmacovigilance Centre is to identify emerging signals from new and existing medicines. In this regard, we have included a feature on a potential signal of pellagra with Isoniazid to watch out for. Whereas the National Drug Authority makes every effort to ensure that the drugs on the market are of good quality and efficacious, the occasional quality issues may arise with products due to pharmaceutical errors or impurities. A report on an ongoing investigation of suspected quality issues with Bupivacaine is included.

In addition, we have included the regular sections on safety updates from manufacturers, the quarterly analysis of adverse drug reactions as well as a unique case of a rare Adverse Event Following Immunization.

We encourage you to send us feedback to these articles through the indicated channels. Enjoy your reading.

*Dr. Helen Byomire Ndagije*



FEEDBACK

***Tel:*** *+256 417 788 100/*
*+256 417 788 124/9*
***Toll Free:*** *0800 101 999*

*+256 791 415 555*

*druginfo@nda.or.ug*

*Uganda National Drug Authority*

*@UNDAuthority*

*www.nda.or.ug*



# SAFETY UPDATES AND PRODUCT LABEL CHANGES

## A. Product information changes for Aluvia and Kaletra

AbbVie, the market authorization holder of Aluvia and Kaletra has updated the package inserts for **Aluvia** 200/50 tablets, **Aluvia** 100/25 tablets and **Kaletra** oral solution to indicate additional contraindications and drug interactions as described below:

**Medicines not to be co-administered with Lopinavir/Ritonavir**

| Class | Drug | Reason |
|---|---|---|
| Anti-cancer agents | Neratinib<br>Vincristine<br>Vinblastine | Serum concentration may be increased by Aluvia, leading to more severe ADRs from the anticancer agent |
| Lipid modifying agents | Lovastatin, Simvastatin, Lomitapide | Aluvia is a CYP3A4 inhibitor. Lomitapide is a substrate for CYP3A4 and usage with Aluvia leads to an almost 27 fold increase in exposure to Lomitapide |

## B. Product information update for Augmentin and Clavulin

GSK, the market authorization holder has updated the prescribing information for **Augmentin and Clavulin** (Amoxicillin and Clavulanic acid) to include aseptic meningitis as a new adverse drug reaction.

**Updated Adverse Reactions:** Reversible hyperactivity, aseptic meningitis, convulsions. Convulsions may occur in patients with renal impairment or in patients receiving high doses.

**Frequency:** The event is reported to have a very rare occurrence

## C. Levitra and increased risk of non-arteritic ischaemic optic neuropathy

Bayer Pharma AG, the market authorization holder of Levitra has updated the Summary of Product Characteristics for its product **Levitra** (Vardenafil monohydrochloride trihydrate) to include results from the analysis of observational data that suggested an increased risk of acute NAION (non-arteritic ischaemic optic neuropathy) in men with erectile dysfunction following exposure to PDE5 inhibitors such as Levitra.

## D. Sanofi Aventis has revised the name of the antigen in Vaxigrip

as part of the annual update for the new strain composition of influenza vaccine for the southern hemisphere influenza season 2020. The SH-2020 has the following strains:

a. An A/Brisbane/02/2018 (H1N1) pdm09-like virus
b. An A/South Australia/34/2019 (H3N2)-like virus
c. A B/Washington/02/2019-like (B/Victoria lineage) virus.

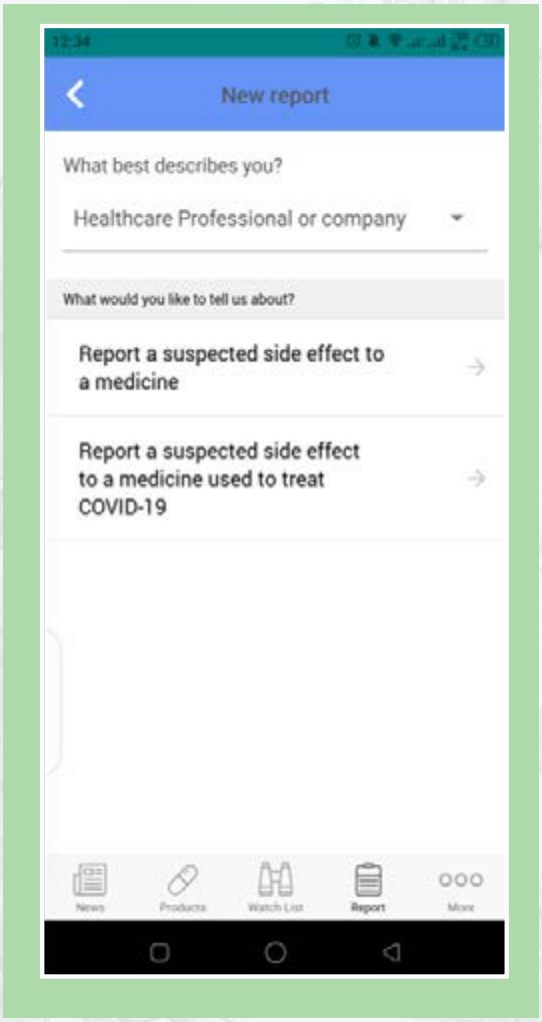
# PHARMACOVIGILANCE DURING COVID -19

In the absence of standard treatment for COVID-19, different countries have systematically evaluated the current available drugs to manage signs and symptoms of the condition.
Uganda is testing and repurposing several drugs for the management of COVID-19 whereas others are being tested in Clinical Trials.

Details of the management guidelines for CoronaVirus can be found in the Ministry of Health publication: "National Guidelines for Management of COVID-19, June 2020".
Given that the doses that may be used in patients with COVID-19 may be higher than those used routinely for the approved indication, the potential for increased risk of side effects is high.

Pharmacovigilance is therefore as important as ever and health workers are encouraged to actively monitor patients for potential side effects .
A specific reporting form has been made available continue reporting through the Med Safety mobile app. Reports of adverse events from both clinical trials and general treatment can be submitted through the app, mail, WhatsApp and physical forms.
Your reports contribute to the characterisation of the safety profile of the repurposed and new medicines in our specific setting and especially for this new illness.
Data from these reports is held in strict confidence and corroborated with findings in other countries so as to make regulatory decisions to keep patients safe.

Download the light and easy to use Med Safety app from Google Play Store or App Store to start reporting today.




REFERENCE
National Guidelines for Management of Covid-19 - COVID-19 | Ministry of Health. (n.d.). Retrieved June 30, 2020, from https://www.health.go.ug/covid/document/national-guidelines-for-management-of-covid-19



# CUTANEOUS DRUG REACTIONS IN HIV POSITIVE PATIENTS ON ISONIAZID PREVENTIVE THERAPY IN UGANDA

**AUTHORS:** Victoria Nambasa, Julius Mayengo, Dr. Fiona Namutebi

The National Drug Authority has received an increasing number of individual case reports reporting various skin changes that have been attributed to isoniazid in people living with HIV. The cutaneous drug reactions have been poorly described by some health workers and misdiagnosed for instance as 'skin rash, severe skin rash, itchy skin rash, skin reactions, hyperpigmentation, erythema, burning sensation' due to lack of knowledge. Without adequate knowledge of the cutaneous drug reactions due to isoniazid, health workers may not be able recognize and institute proper management. This may have substantial impact on patient willingness to accept or complete therapy. We present a description and expert clinical characterization of skin reaction received by NDA.

## DESCRIPTION OF THE ISONIAZID ASSOCIATED CUTANEOUS LESIONS

One hundred individual case safety reports of HIV positive patients on IPT from various health facilities in the country from March 2016 to June 2020 were reviewed. Nine cases were excluded because they predominantly had systemic involvement e.g. drug induced liver injury, hemolysis, neuropathy and nonspecific symptoms. Ninety-one individual case safety drug reports of cutaneous adverse events were subsequently reviewed.

Of the 91 individual case safety drug reports reviewed, females 82 (90.1%) were the most affected with an average age (SD) of 36.4 (10) years.

Majority 60 (60.6%) of the cutaneous lesions were clinically consistent with pellagra. Other descriptions were suggestive of maculopapular eruptions (12 cases), pruritus (6 cases), urticaria (5 cases), Steven Johnson Syndrome (4 cases), bullous drug reactions (2 cases), exfoliative dermatitis (1 case) and erythema multiforme (1 case) (Figure 1)

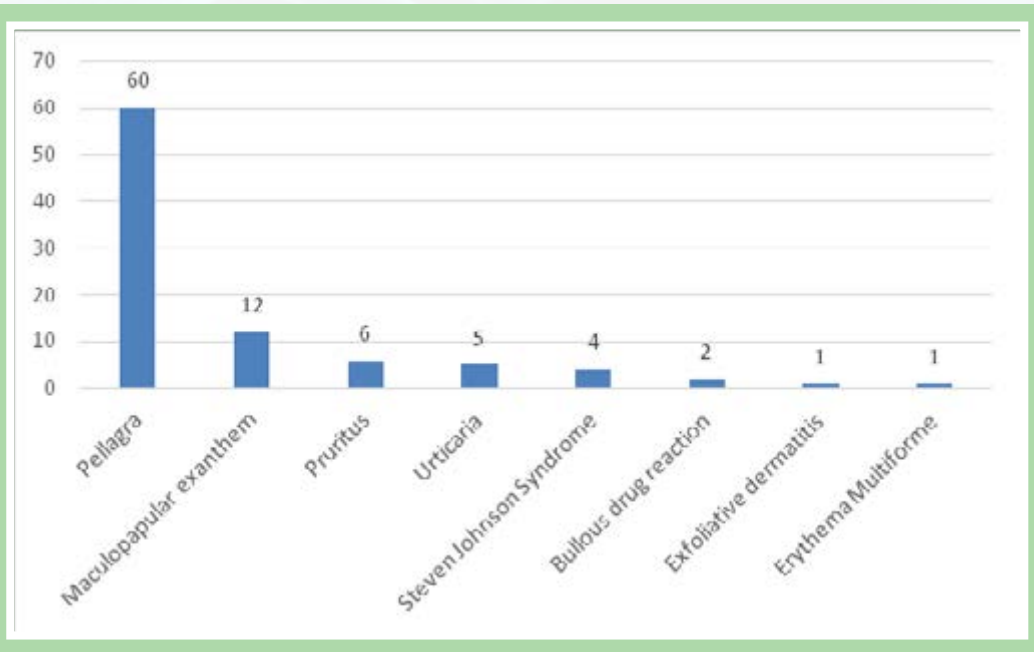


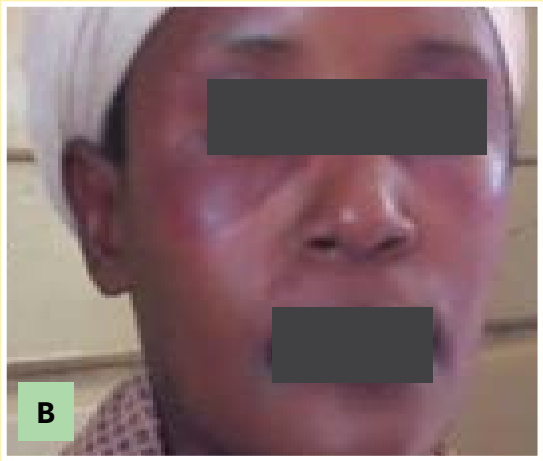

*Figure 1: Spectrum of Isoniazid associated adverse Cutaneous Drug eruptions.*

Isoniazid associated pellagra was the commonest cutaneous manifestation and the most poorly described by the health workers. Of the 60 patients with pellagra majority were females 56 (61.5%) with a mean age (SD) of 35.6 (7.8). The median time to developing pellagra was 45 days. An interaction with some patients at one of the health centers in Kampala revealed diets lacking in niacin e.g. meat.

Several patients were reported to have a preceding burning sensation of the skin before the rash onset. The skin lesions were mostly distributed on sun exposed areas i.e. the face, neck, upper chest, lateral forearms, dorsum of the hands, feet and lips. The rashes were symmetrical erythematous or hyperpigmented patches and scaly plaques, sharply demarcated from the normal skin especially on the dorsum of the hands and lateral forearms (images 1A & B). Other manifestations included edematous and erythematous acneiform plaques in the butterfly region of the face, a violaceous heliotrope like rash around the eyes (images 2A &B), the classic Casal necklace (image 3B); hyperpigmented eczematous plaques with crusting and fissures involving the dorsum of the hands and wrists (image 4); cheilitis and oral sores (image 5 A), hypo-pigmented annular plaques on the dorsum of the hands (images 5 B& C); brown scaly annular plaques on the palms (images 5 D&E).

Three patients were reported to have diarrhea and one patient was reported to have poor concentration and forgetfulness. No death due to isoniazid associated pellagra was reported.

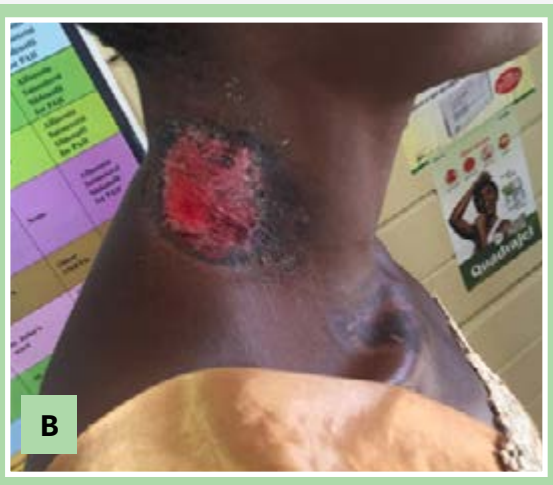
Image 1


**A.** Shows edematous erythematous plaques in the butterfly region of the interspersed with acneiform lesions
**B.** A violaceous rash around the eyes ('heliotrope'like rash)

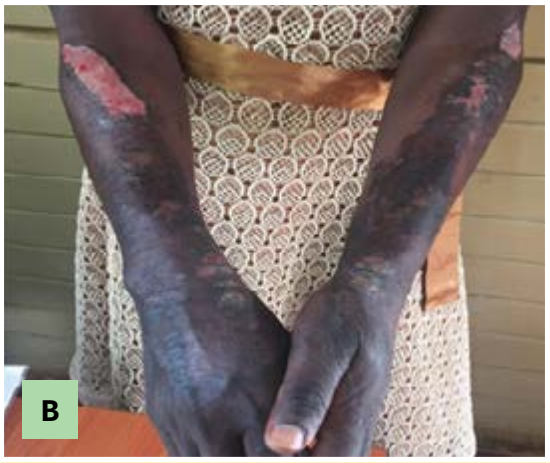


Image 2


**A.** The 'V' region of the neck shows a well demarcated brown patch with superficial scaling at the edges.
**B.** Shows well demarcated band like scaly hyperpigmented plaques around the neck consistent with the 'Casal necklace' with areas of denuded skin.

Image 3

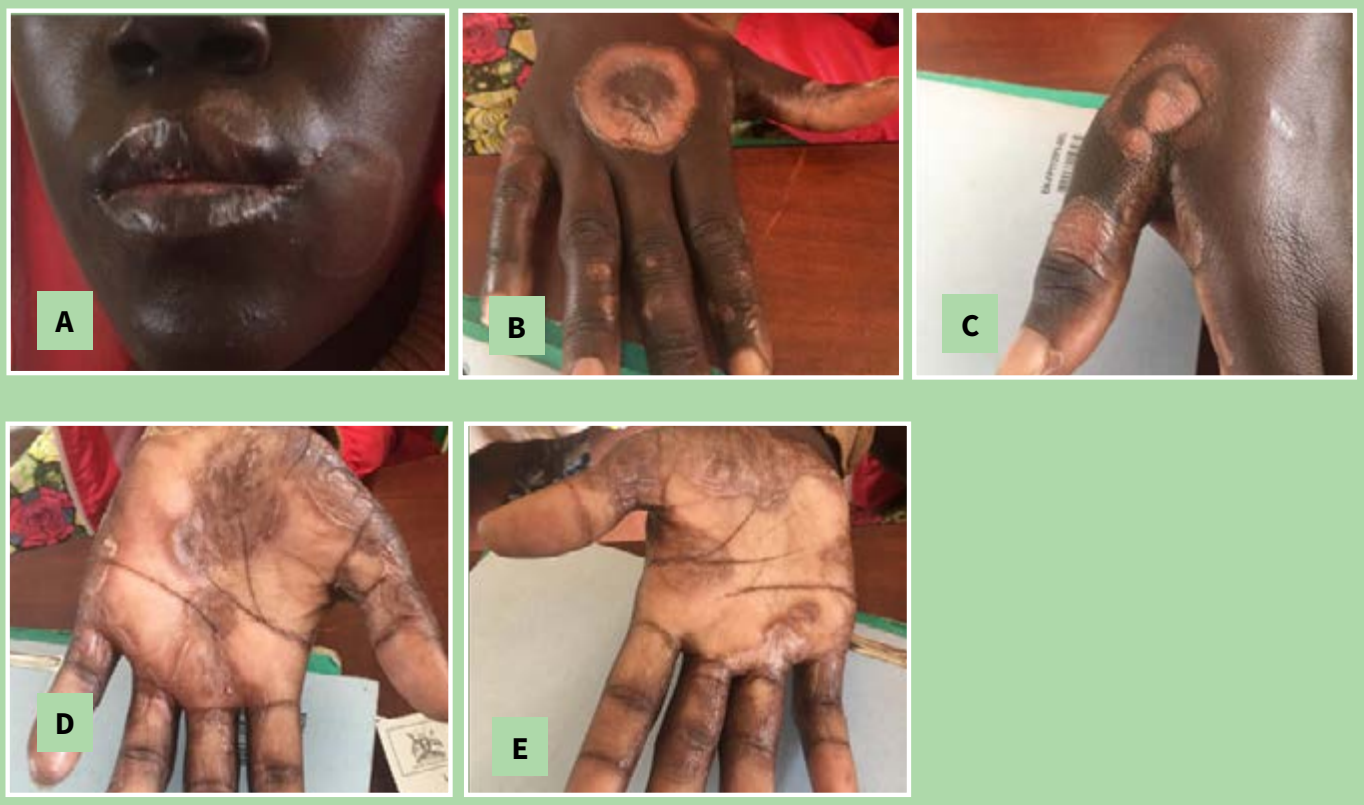




**A.** Early lesions on the dorsum of the hands showing ill-defined hyperpigmented patches.
**B.** Bilateral symmetrical hyperpigmented scaly plaques on the lateral forearm skin and dorsum of the hands interspersed with denuded skin.

Image 4

**Wrists**
Well demarcated bilateral and symmetrical eczematous hyperpigmentedlichenified plaques with fissures.

Image 5




**A, B, C, D** and **E** belong to the same patient
**A:** Oral sores, cheilitis with perioral annular hypopigmented patches especially at the periphery
**B & C:** Hypopigmeneted annular plaques on the dorsum of the hand
**C & D:** Hyperpigmented annular scaly plaques on the palms. There is need to rule out syphilis in this patient

## DISCUSSION

Isoniazid associated pellagra was the predominant cutaneous manifestation and the most poorly described by the health workers in the cases evaluated. An interaction with some patients at one of the health centers in Kampala revealed diets lacking meat. However, the numbers were too small to make a conclusion on dietary intake of niacin containing foods.

According to Summary of product Characteristics (SmPC)[1] for Isoniazid, Pellagra is listed as an adverse drug reaction with unknown frequency of occurrence. In addition, skin and subcutaneous disorders including erythema multiform, Purpura, Rash, Exfoliative dermatitis are listed as well but with unknown frequency of occurrence.

HIV infection is associated with low levels of tryptophan and hence pellagra[2]. Isoniazid (INH) interferes with niacin synthesis and may induce pellagra in susceptible patients e.g. the malnourished, alcoholics and those on isoniazid therapy[3]. Isoniazid induced pellagra was first reported in the British Medical Journal in a female patient with poor food intake who isoniazid to treat disseminated sclerosis[4].



Pellagra is characterized by the four "D's":dermatitis, diarrhea, dementia and death in about 5 years of untreated disease[5]. Skin changes manifests upon exposure to sunlight and pressure. The disorder classically begins with a symmetric itching and smarting erythema on the dorsa of the hands, neck, and face. Vesicles and bullae may erupt and break, so that crusting occurs and lesions become scaly. Later, skin becomes indurated, lichenified, rough, covered by dark scales and crusts; there are cracks and fissures and a sharp demarcation from normal skin.

The tetrad of pellagra was not manifested in the majority patients. However, the cutaneous manifestations were all present in our patient population. Three patients were reported to have diarrhea and one patient was reported to have poor concentration and forgetfulness. No death was reported probably because of the short 6-month duration of IPT given to the patients.

Pyridoxine is essential in tryptophan metabolism which results in the formation of niacin[6].However, isoniazid-induced pellagra may occur despite pyridoxine supplementation[7].
Figure 2 shows the basic metabolic pathway of tryptophan metabolism. It is hypothesized that isoniazid inhibits synthesis of NAD and NADP by a competitive inhibition mechanism. Nicotinamide, isoniazid and pyridoxine are all structurally similar with ring of five carbon atoms and one nitrogen at position four[2] (Figure 3). In susceptible individuals, an appropriate mutation of the enzyme may be sufficient to interfere with NAD/NADP. It is suggested that isoniazid competes with nicotinamide for its site of action[3].

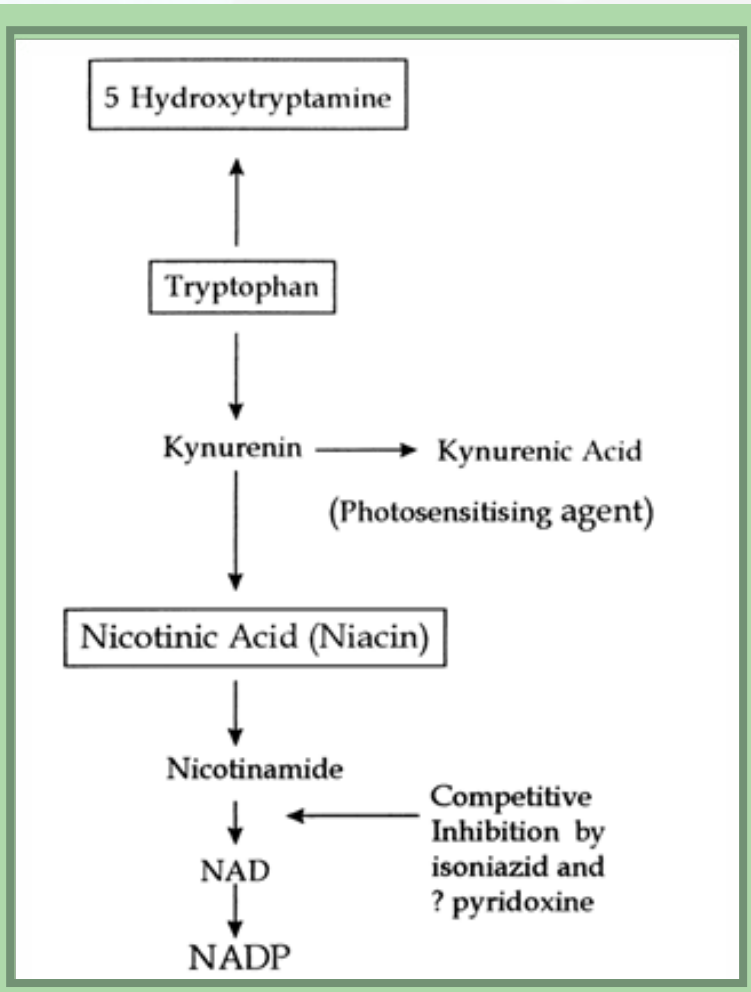



*Figure 2 : Basic biochemical pathway of tryptophan and niacin metabolism.*

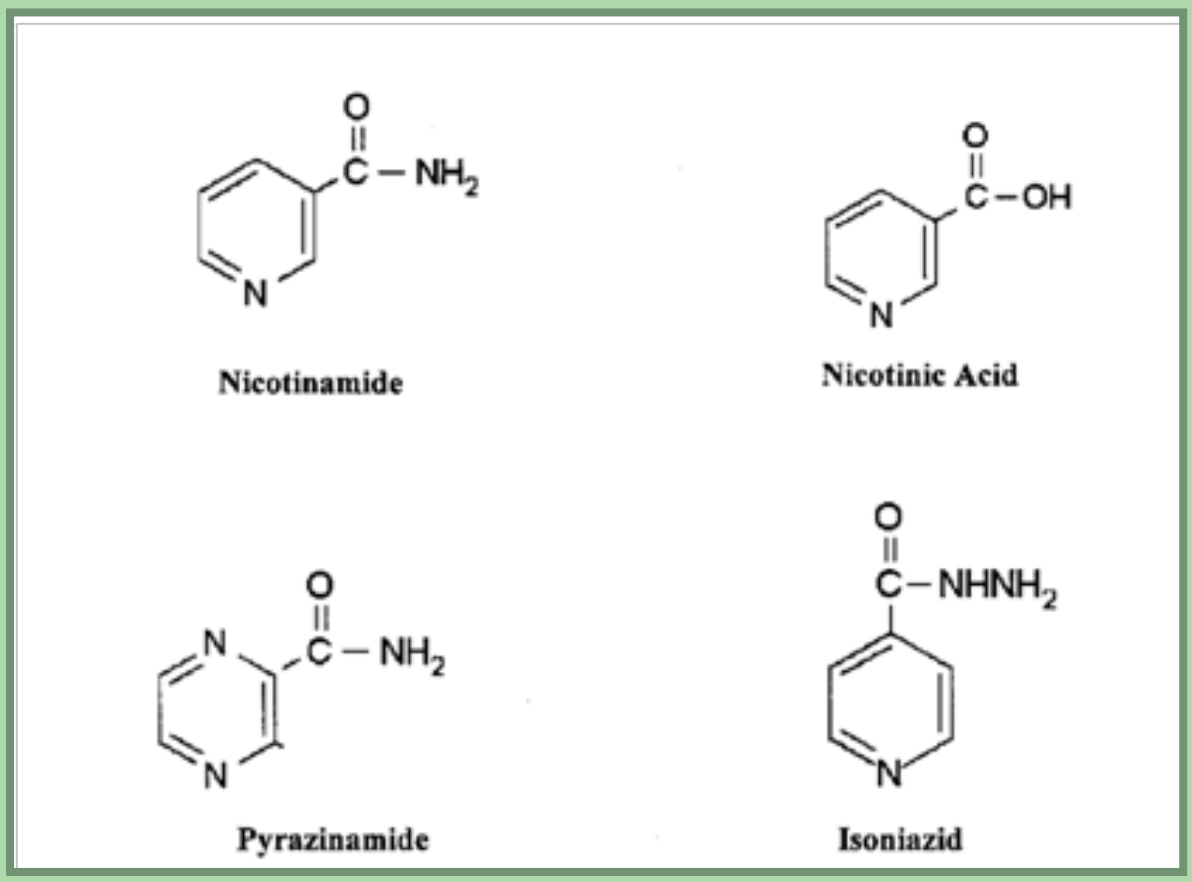



*Figure 3 : Structure of nicotinamide and related compounds*

## CONCLUSION

Isoniazid induced pellagra is on the rise amongst HIV positive patients on Isoniazid Preventive Therapy.

### RECOMMENDATIONS

1. Patients should be advised on appropriate dietary intake, sun protection and counseling on pellagra related skin manifestationsshould be emphasized among PLHIV taking INH.
2. Patients should be given routine pyridoxine supplementation while on INH.
3. For established cases, oral administration of nicotinamide plus other vitamins of the B complex cures the disease.Other manifestations of pellagra should be assessed and differential diagnoses ruled out,
4. For serious cases, a referral to a Dermatologist may be required.



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# Serious Adverse Reactions Following Use of Bupivacaine Hydrochloride(NETVAICAIN) in batch SX-19352

The National Drug Authority has received 20 reports of serious adverse events that occur following the administration of Bupivacaine Hydrochloride in Dextrose batch SX-19352 (NETVAICAIN). The adverse reactions cases occurring in caesarian mothers present as headache, vomiting, confusion, drowsiness, and profuse sweating. In some cases, there was dyspnoea, depressed level of consciousness, restlessness, and cardiac arrest. On average, most of the events occurred 5 hours after administering the drug intrathecal. All the facilities that reported have similarly indicated no incidents with other brands of bupivacaine.

Bupivacaine Hydrochloride is used for the production of local anesthesia by percutaneous infiltration, peripheral nerve block(s) and central neural block (caudal or epidural), that is, for specialist use in areas where prolonged anesthesia is indicated.


Samples of the suspected Bupivacaine

## LITERATURE AND LABELED INFORMATION:

The literature, specifically the summary of product characteristics for Bupivacaine indicates confusion to be a rare known/labeled adverse drug reaction of Bupivacaine. Headache and neck pain are not well described but have been reported in some few case reports. Within the global pharmacovigilance database, 394 cases of headache, 781 cases of varying pain and 112 cases of confusion have been reported. The reports vary in severity.

Based on the information provided in the reports, and that drawn from other cases received, it is probable that Bupivacaine could have caused the events. Given the specificity of all the reported events to a specific batch of a particular brand, this is likely to be related to the quality of the drug. Consequently, results from quality testing will be useful to rule out quality issues that could account for the event. NDA will share with you a formal communication once the results from these investigations are completed.

**RECOMMENDATIONS**

You are advised to quarantine this product and consider using other brands of bupivacaine pending further guidance from NDA.

REFERENCE

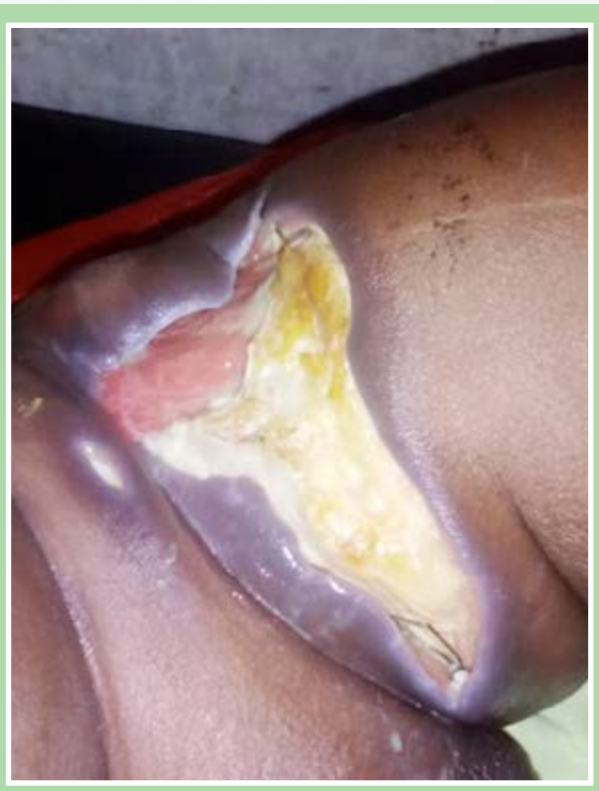
emc-Bupivacaine (SPmC) https://www.medicines.org.uk/emc/product/3619/smpc



# CASE REPORT: ADVERSE EVENT FOLLOWING IMMUNIZATION

## CELLULITIS AT PENTAVALENT VACCINE (DTP-HEPB-HIB) ADMINISTRATION SITE

K.M is an 8 months old male infant who presented to a health facility in Uganda with fever (39°C) and a history of swelling of the left Upper thigh. Medical History revealed that he had been injected with a third dose of pentavalent vaccine (DPT-HEPB-HIB) a day before the symptoms presented. The swelling gradually increased in size and burst exposing an ulcerative lesion. A physical examination revealed fontanelle bulging and septicemia. The child was diagnosed with cellulitis of the left thigh with abscess. Incision and Drainage was done and the patient is being managed for pyomyositis.



Cellulitis is a non-necrotizing inflammation of the skin and subcutaneous tissues, a process usually related to acute infection that does not involve the fascia or muscles. It is characterized by localized pain, swelling, tenderness, erythema, and warmth.1 The Pentavalent (DTP-HepB-Hib) vaccine is a combined vaccine containing diphtheria and tetanus toxoids, Bordetella pertussis inactivated cellular suspension, hepatitis B surface antigen (HBsAg), and Haemophilus influenzae type b conjugated oligosaccharide.[2] The product is administered as an intramuscular injection in the anterolateral thigh as a primary or booster dose for immunization of infants and toddlers against diphtheria, tetanus, pertussis, hepatitis B, and invasive illness caused by H. influenzae type b.[2] The vaccine is indicated for infants regardless of whether or not they have received hepatitis B vaccination at birth.[2]

## LABELLED REACTIONS

Commonly described local adverse reactions following Pentavalent vaccination with >1/100 frequency of occurrence include diarrhoea, vomiting, injection site reactions (erythema, induration, pain), feeding disorders and irritability[2].

## LITERATURE

According to a study conducted by Nguyen in 2013, during the roll out of the pentavalent vaccine in Hanoi, local reactions reported including swellings, redness, pain were found in 0.11%, 0.09%, and 0.03% of recipients, respectively. The adverse events occurred sporadically, and mainly occured within 6 hours after

injection. All minor cases were completely recovered.[3] The National Drug Authority AEFI line listing of 2020 has three cases due to routine immunization with pentavalent vaccine. These cases are all expected and include injection site abscess and cellulitis.

## DISCUSSION

Injection site reactions (ISRs) such as cellulitis are common adverse events following immunization with pentavalent vaccine[4]. The risk of ISRs varies according to the injection site, the product and the dose number[(4, 5)]. These reactions usually resolve with symptomatic treatment and do not contraindicate the use of the product[(4, 5)].

According to Rennels 2003, extensive local reactions usually occur after administration of the fourth and fifth booster doses of diphtheria-tetanus-acellular pertussis (DTaP) vaccines. The incidence of these occurs in 2 to 6 percent of children given booster doses of DTaP vaccines. The reactions subside without sequelae, but they may be misdiagnosed as cellulitis and lead to unnecessary medical intervention. The pathogenesis of these reactions probably is multifactorial. Evidence suggests that both antigen content and pre vaccination immunity have roles. Important, unanswered questions are the safety of revaccinating a child who previously has had an extensive local reaction and the safety of introducing further DTaP boosters into the adolescent and adult populations.[5]

RECOMMENDATIONS

- Advise mothers to monitor children after vaccination to help in early detection and management.
- Take detailed patient history to avoid administering medicines to patients who may be allergic.

REFERENCES

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# HAEMOVIGILANCE

## OVERVIEW

Blood products are scheduled as class B group II drugs as per the National Drug Policy and Authority act, cap 206. The objective of this regulation is to ensure that blood and blood products for human use are safe, pure, potent, effective and appropriately labelled.

Essential blood and blood components include but are not limited to: whole blood, Red Blood Cells, Platelets and Plasma. Plasma may include convalescent plasma as in the case of COVID-19 where it has been tested as a possible treatment.

Haemovigilance is a continuous process of data collection and analysis of transfusion-related adverse events and reactions (AR/AE) in order to investigate their causes and outcomes, and prevent their occurrence or recurrence. A haemovigilance system is an integral part of quality management in a blood system and is required for the continual improvement of the quality and safety of blood products and the transfusion process. Haemovigilance is essential to identify and prevent the occurrence or recurrence of adverse reactions and unwanted events, and to increase the safety, efficacy and efficiency of blood transfusion. It covers all activities of the blood chain, vein-to-vein, from donor to recipient.

## TRANSFUSION CHAIN

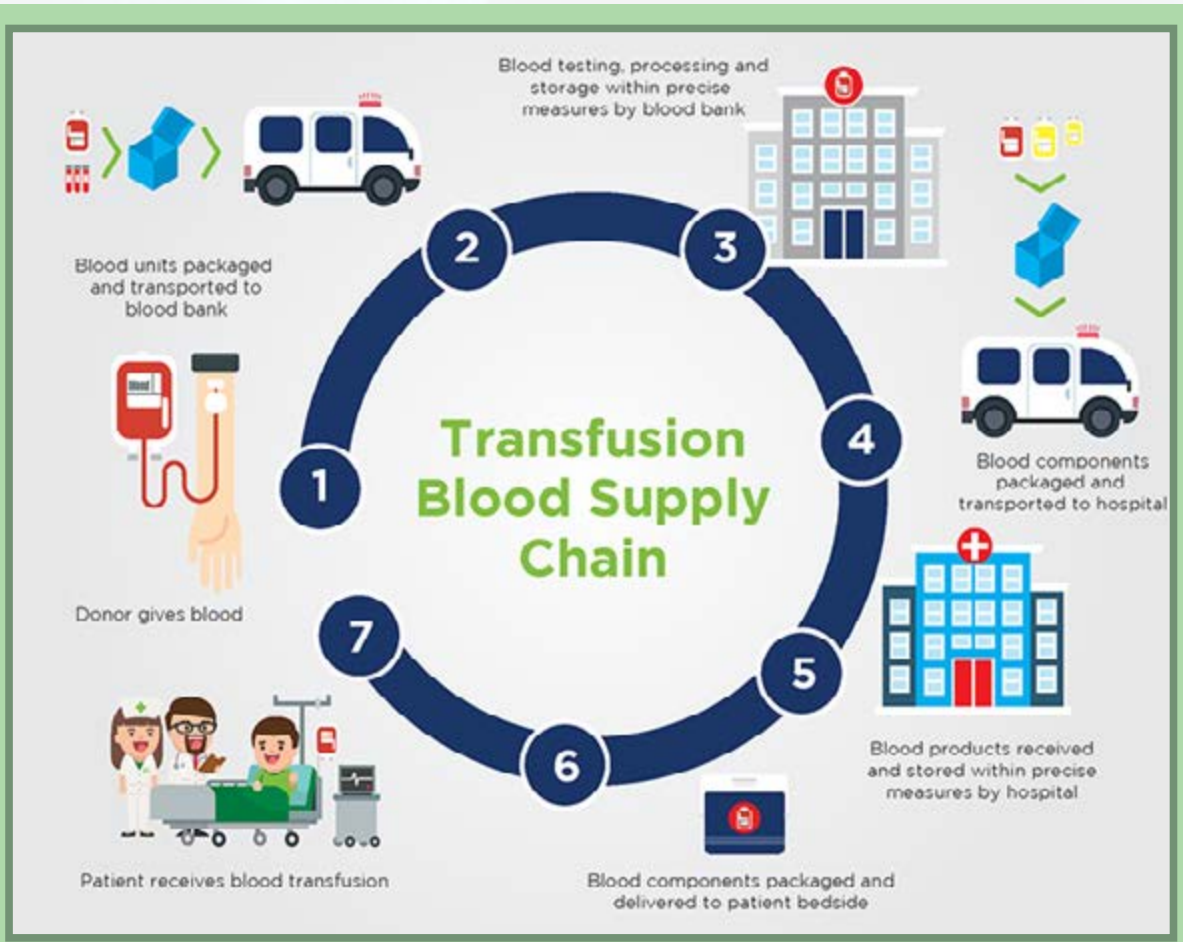
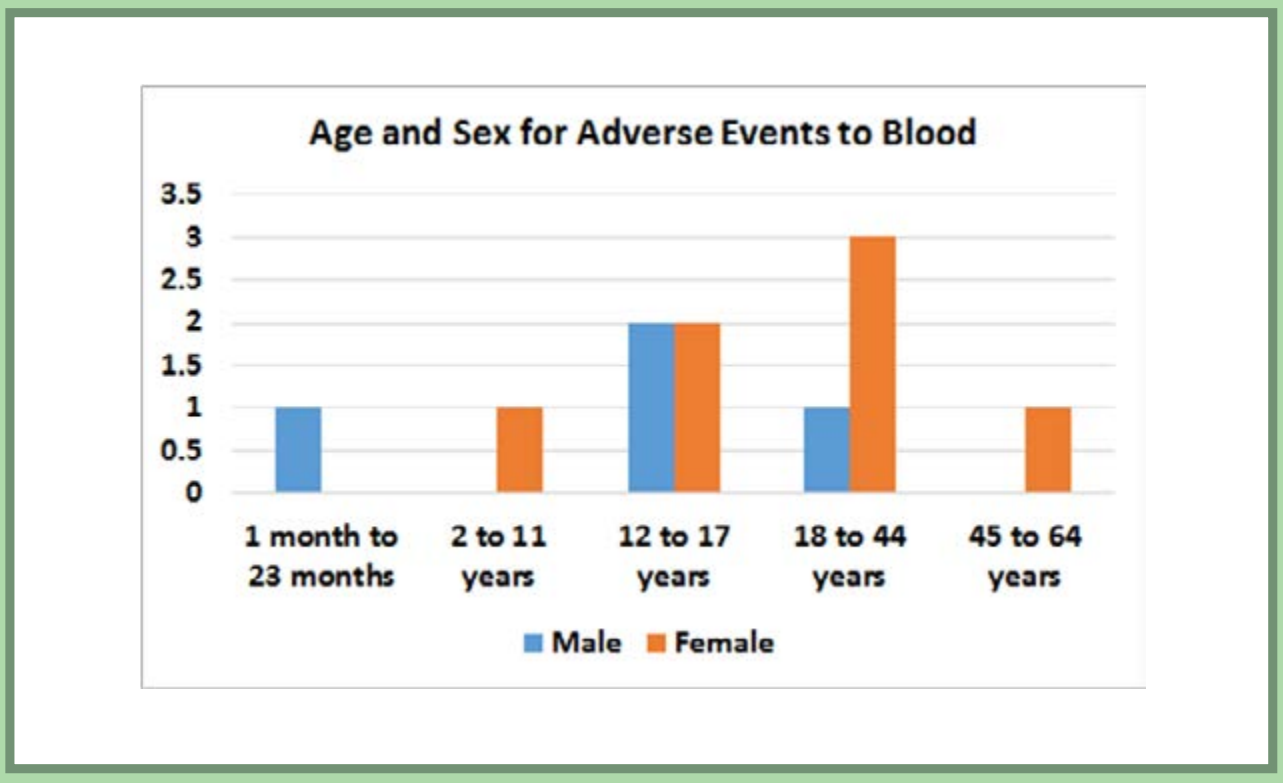



*Image source: https://www.packmaxq.com/post/the-challenges-of-the-blood-supply-chain*

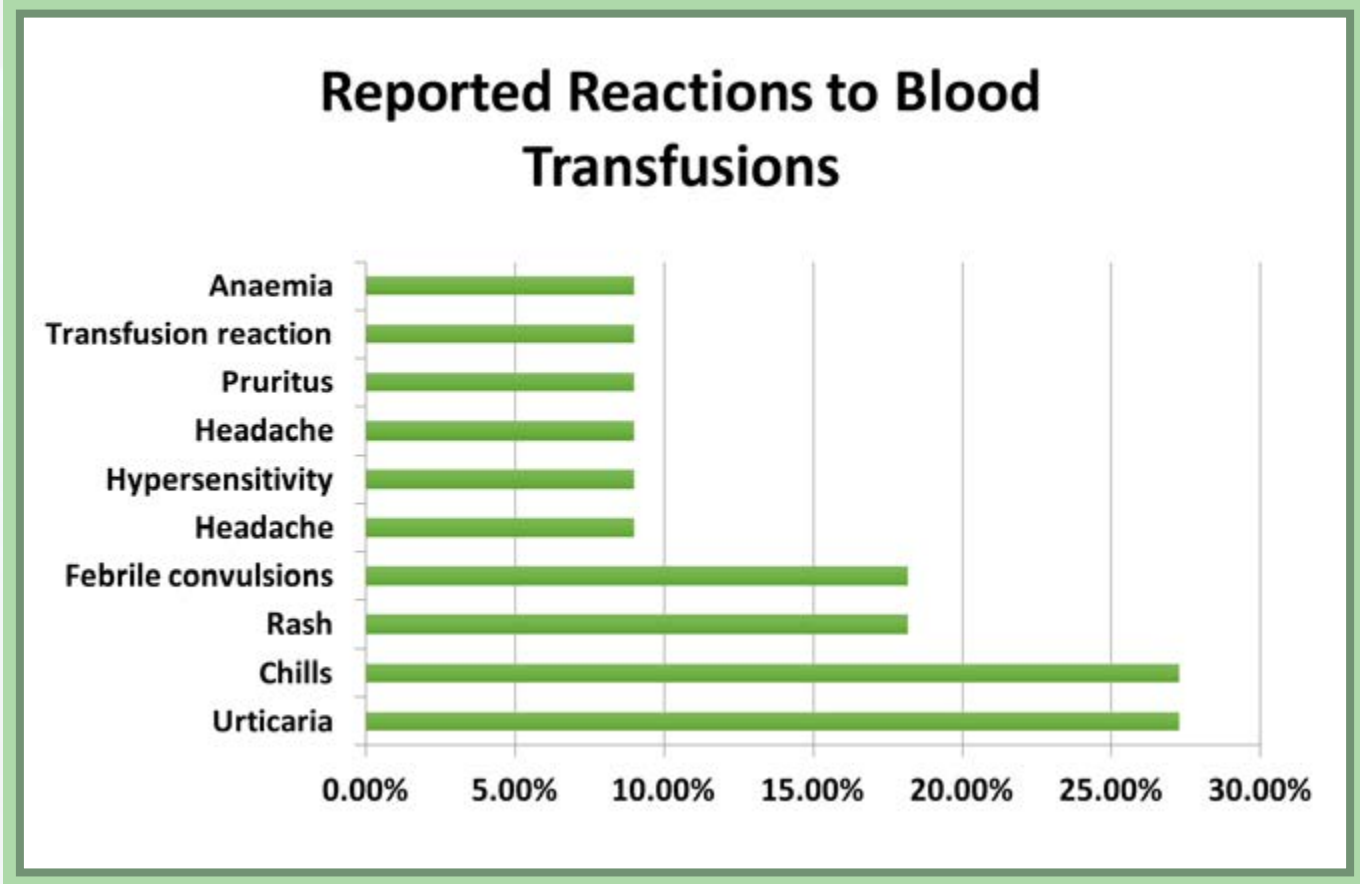
The causes of transfusion adverse events are found along the transfusion chain and therefore the involved health care professionals (doctors, nurses, laboratory scientists) are all responsible for identifying, reporting and preventing these reactions.

## TRANSFUSION REACTIONS REPORTED TO NDA

Since 2006, the National Drug Authority has received 11 reports of adverse drug events to blood transfusions. Over half of the reports were from Infants, children and adolescents as compared to adults. 63% of the affected patients were female.








Majority of the reactions were classified as skin and subcutaneous tissue disorders due to sudden development of an itchy skin rash.
All the reactions were reported to be due to whole blood.

**RECOMMENDATIONS FOR PREVENTION**

Acute reactions may occur in 1-2% of patients but rapid recognition and management of these may save the patient's life. Follow the recommended Uganda Clinical Guidelines in observing, recording and reporting any possible reactions.

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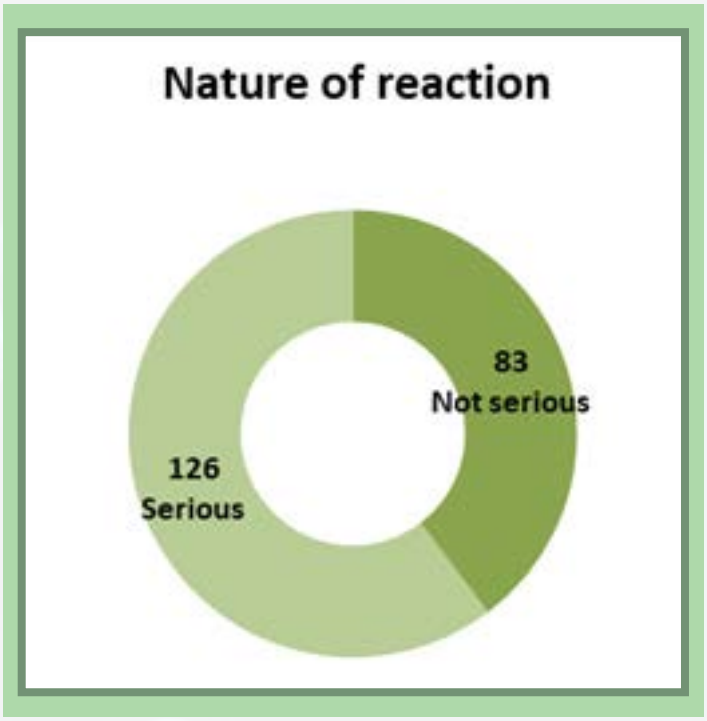
3. A guide to establishing a National haemovigilance system, World Health Organization, 2016
4. Uganda Clinical Guidelines, Ministry of Health, 2016
5. Swissmedic vigilance news, edition 19- November 2017

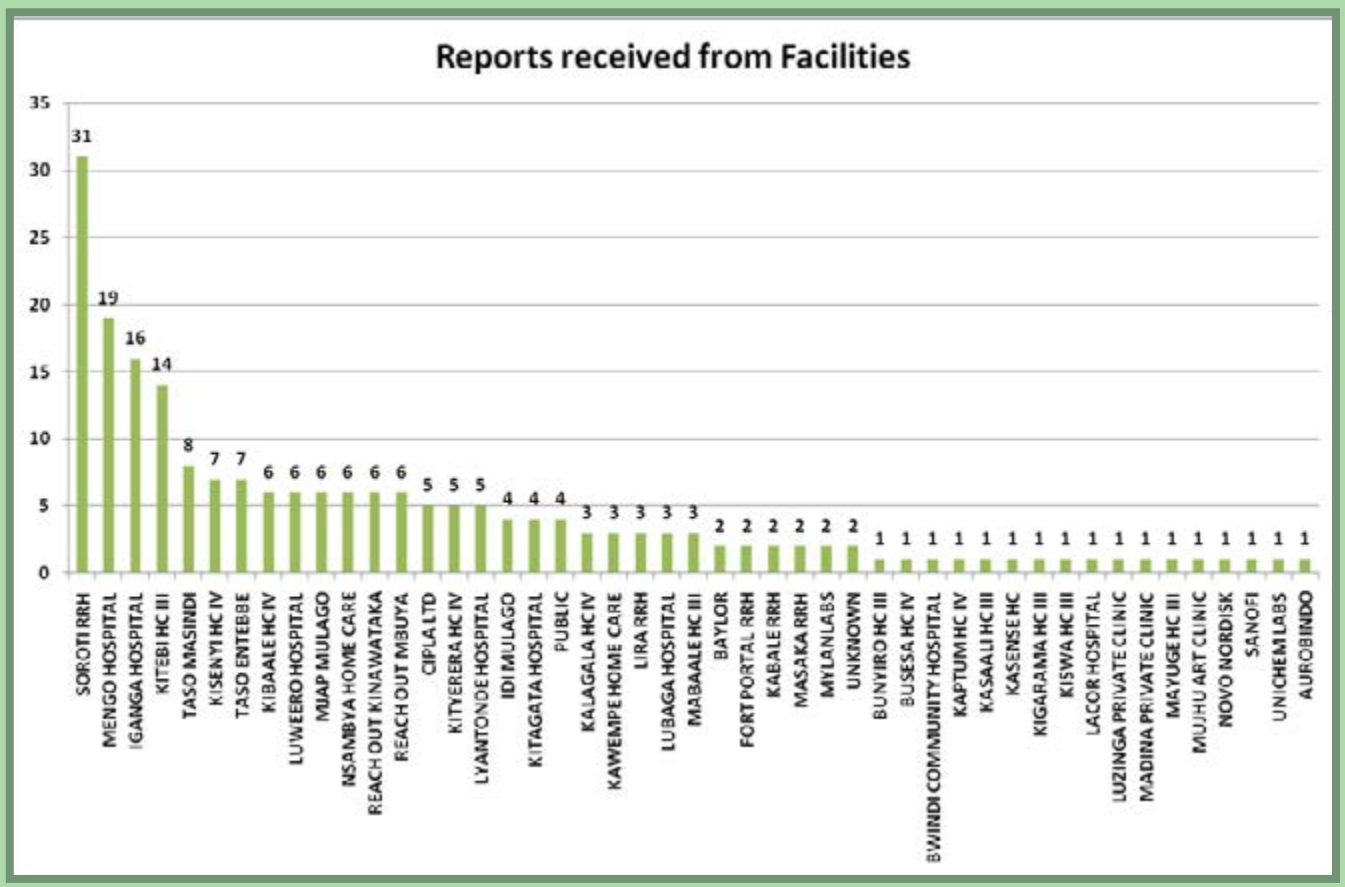


# ADR REPORTING STATISTICS

In the period from 1st April to 30th June 2020, the National Drug Authority received a total of 209 reports.

Of these 209 reports 126 (57%) were graded as serious.



## TOP DRUGS AND REACTIONS

| Drug | Total Reports | Top Reactions | |
|---|---|---|---|
| Isoniazid | 78 | Severe generalized skin reaction with hyperpigmentation | 35 |
| | | Jaundice | 4 |
| | | Pellagra | 3 |
| Dolutegravir | 35 | Hyperglycaemia | 13 |
| | | Erectile dysfunction | 4 |
| | | Insomnia | 3 |
| Bupivacaine | 21 | Mental confusion, restlessness, aggression, uncoordinated speech | 21 |
| Efavirenz | 15 | Excessive dizziness, drowsiness, general body weakness | 8 |
| | | Hypersentivity skin reaction | 2 |
| | | Peripheral neuropathy | 2 |
| Lidocaine | 13 | Lack of efficacy | 12 |
| | | Fainting | 1 |
| Tenofovir | 5 | Osteoporosis | 2 |
| | | Renal toxicity | 2 |
| | | Chronic liver disease | 1 |
| Amphotericin B | 4 | Generalised tonic clonic seizure | 1 |
| | | Electrolyte imbalance | 2 |
| Atazanavir/Ritonavir | 3 | Jaundice | 3 |
| Nevirapine | 3 | Skin reaction | 2 |
| | | Generalised skin rashes, itching and swelling of eyes, dysphagia, photophobia | 1 |
| Dpt/Hib/Hep | 3 | Abscess | 1 |
| | | Inflammation, Nodular mass | 1 |
| | | Fever, septiceamia, bulging of frontanelle, cellulitis | 1 |
| Chlorpromazine | 2 | Itchy skin rash | 2 |



**NATIONAL DRUG AUTHORITY**
Plot No. 19 Lumumba Avenue,
P.O. Box 23096, Kampala, Uganda.
Email: ndaug@nda.or.ug; druginfo@nda.or.ug
website: www.nda.or.ug
Tel: +256-414-255665, +256-414-347391/2

Doc. No.: DPS/FOM/313
Revision No.: 0
Effective Date: 11 Mar 2019



# SUSPECTED ADR/AEFI REPORTING FORM

*Note: Reporters and patients identity are held in strict confidence by NDA and protected to the fullest extent of the law*

**Type of Report**

Initial ☐ Follow up ☐ | Serious ☐ Not Serious ☐ | Drug ☐ Vaccine ☐

**Patients Information**

Patient ID/initials: _____ Gender: Male ☐ Female ☐ Weight (kg)_____ Pregnancy status Yes ☐ No ☐ N/A ☐

Full address_____ Telephone Number _____

*Date of birth :_ _/_ _/_ _ _ (dd/mm/yyyy) OR Age at onset:*_____ Medical History _____

**Vaccine(s) Information**

| ***Vaccine*** | | | | | | ***Diluent (if applicable)*** | | | |
|---|---|---|---|---|---|---|---|---|---|
| Name of vaccine | Date of vaccination | Time of vaccination | Dose (1st, 2nd, 3rd etc) | Batch/Lot Number | Expiry date | Name of diluent | Batch/Lot Number | Expiry date | Date and time of reconstitution |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |

**Medical Product Details**

| **List of all medicines used in the last 3 months** | **Brand name** | **Batch no** | **Route, Dose and frequency** | **Date started** | **Date stopped** | **Indication** | **Tick suspected medicine** |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

**Brief description of the ADR/AEFI and any treatment given**

**Description of the AEFIs** *(for vaccines)*
Severe local reaction > 3 days ☐ Encephalopathy ☐ Toxic shock syndrome ☐ Thrombocytopenia ☐ Anaphylaxis ☐ Generalized urticaria (hives) ☐ Injection site abscess ☐ High fever ≥38 ℃ ☐
Other (specify) _____

Date of ADR/AEFI onset: _ _/_ _/_ _ _ _ Time of onset: _____ Date ADR/AEFI stopped: _ _/_ _/_ _ _ _

**Severity of the ADR/AEFI**
Mild ☐ Moderate ☐ Severe ☐ Fatal ☐ Unknown ☐

**Reason for seriousness**
Prolonged hospitalization ☐ Congenital anomaly ☐ Disability ☐ Death ☐ Life threatening ☐

**Action taken**
Drug withdrawn ☐ Dose increased ☐ Dose reduced ☐ Dose not changed ☐ Not applicable ☐ Unknown ☐

**Outcome**
Recovered ☐ Recovering ☐ Continuing ☐ Recovered with sequelae ☐ Not recovered ☐ Death ☐ Unknown ☐

**Causality of the ADR/AEFI**
Certain ☐ Probable/ Likely ☐ Possible ☐ Unlikely ☐ Unclassifiable ☐

**Reporter details**

| Name of reporter: | E mail Address/Contact:<br>Designation: | Date of reporting |
|---|---|---|
| Institution/Health facility: | Contact/Email: | District: |

**Administrative details**

| Report title: | Form ID number: | Date received: |
|---|---|---|

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# SUSPECTED ADR/AEFI REPORTING FORM

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## Guidance on reporting

**What to report**

Report all adverse drug reactions/events suspected both serous and those that are not serious.
Report any adverse reaction or AEFIs even if you are not certain the product caused the event

**When To Report**

For serious ADRs within 24-48 hrs.' of notification
For AEFIs report immediately you are notified
For non-serious events as soon as possible but not later than 15 days

**Who Is To Report**

- All Healthcare Providers should report as part of their professional responsibility any suspected adverse drug reactions and AEFIs

**Where To Report**

- reports should be sent to the National Drug Authority
- reports can also be sent to the national AEFI committee

**How to report**

- fill in the sections that apply to your report
- Start date of administration for the suspected drug and the date when the suspected reaction occurred

**Severity of reaction**

**Mild**: ADR/AEFI that requires no change in treatment with the suspected drug. Requires suspected drug to be withheld, discontinued or otherwise changed. No prolonged hospitalization

**Moderate:** ADR/AEFI requires the suspected drug to be withheld, discontinued or otherwise changed. Prolongs hospitalization by at least 1 day. ADR is the reason for admission

**Severe:** ADR/AEFI requires intensive medical care, causes permanent harm to the patient

**Fatal:** ADR/AEFI either directly or indirectly leads to death of the patient

**Detection of ADR/ AEFIs in a Patient**

Follow the following steps

- Take proper history and conduct proper examination of the patient.
- Ensure that the medicine ordered is the medicine received and actually taken by the patient at the dose advised.
- Verify that the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation made by the patient.
- Determine the time interval between the beginning of drug treatment and the onset of the event.
- Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient's status (De-challenge). If appropriate, restart the drug treatment and monitor recurrence of any adverse events (Re-challenge).
- Analyze the alternative causes (other than the drug) that could on their own have caused the reaction.
- Use relevant up-to date literature and personal experience as a health professional on drugs and their ADRs and verify if there are previous conclusive reports on this reaction

**Please note** that submission of a report doesn't imply that the health worker or the product caused or contributed to the adverse event

**WHO-UMC causality assessment scale**

| Causality Term | Assessment |
|---|---|
| Certain | • Event of laboratory test abnormality, with plausible time relationship to drug intake<br>• Cannot be explained by disease or other drugs<br>• Response to withdrawal plausible (pharmacologically, pathologically)<br>• Event definitive pharmacologically or phenomenologically *(i.e. an objective and specific medical disorder or a recognized pharmacological phenomenon)*<br>• Rechallenge satisfactory , if necessary |
| Probable | • Event or laboratory test abnormality, with reasonable time relationship to drug intake.<br>• Unlikely to be attributed to disease or other drugs<br>• Response to withdrawal clinically reasonable<br>• Rechallenge not required |
| Possible / likely | • Event or laboratory test abnormality, with reasonable time relationship to drug intake<br>• Could also be explained by disease or other drugs<br>• Information on drugs withdrawal lacking or unclear |
| Unlikely | • Event or laboratory tests abnormality, with a time to drug intake that makes a relationship improbable (but not impossible)<br>• Disease or other drugs provide plausible explanations |
| Conditional / Unclassified | • Event or laboratory test abnormality<br>• More data for proper, assessment needed or<br>• Additional data under examination |
| Not assessable / unclassifiable | • Report suggesting an adverse reaction<br>• Cannot be judged because of insufficient or contradictory information<br>• Data cannot be supplemented or verified |

**Confidentiality**

All information pertaining to the reported event should at all times be treated in confidence and protected from an authorized access transmission of use.



# WHAT IS **PHARMACOVIGILANCE**

Pharmacovigilance" refers to the science and activities concerned with the knowledge, detection, assessment, understanding and prevention of adverse reactions to medicines or any drug-related problems.

The major aims of Pharmacovigilance are

1. Early detection of previously unknown adverse reactions and interactions.
2. Detection of increase in known adverse drug reactions.
3. Identification of predisposing risk factors and possible mechanisms underlying adverse reaction.
4. Estimation of quantitative aspects of risk/ benefits analysis and dissemination of needed information to improve drug prescribing, use and regulation.

Role of national pharmacovigilance center at NDA. Every single case of adverse drug reaction that is received helps NDA to monitor the safety of medicines. The staff analyze the case reports regularly to look at the relationship between medicines and side-effects. When we identify a possible new link between a medicine and a side effect we quickly look into it to see if there is a problem. If there are any new potential risks identified, NDA takes action to minimize these risks and protect the public. Action taken may include:

- we may require the manufacturer to update the information on how the medicine should be used
- rarely Recall or withdraw of medicine from the market
- Restricted use of the medicine
- Safety communication to the healthcare providers, drug companies or the public

**CALL FOR REPORTING**

Please remember that you can report suspected adverse reaction to medicines, and adverse reaction following immunization to NDA using the following channels: Med Safety app, email: **druginfo@nda.or.ug, whatsapp: 0791415555, toll free: 0800101999** and hard copy forms delivered to any of our offices.

# NATIONAL DRUG AUTHORITY HEAD OFFICE AND REGIONAL OFFICE CONTACTS

**NATIONAL DRUG AUTHORITY**
Head Office, Plot 46 - 48 Lumumba Avenue
P.O. Box 23096, Kampala, Uganda
Tel: +256 414 255665, +256 414 347391/2
+256 417 788100/1, +256 417 788124/9
Toll Free: 0800 101 999

**NATIONAL DRUG QUALITY CONTROL LABORATORY**
Tel: +256 414 540 067

**CENTRAL REGION NAKAWA**
Premier Engineering works Ltd,
Premier Complex, Plot 1-2, Enterprise Close
Jinja Road, Ntinda Industrial Area,
Tel: +256 393 261548/ 312 261548

**WEST NILE REGION, ARUA**
Plot Mount Wati Avenue, Arua Municipal council
Tel: +256 414 671033

**NORTHERN REGION, LIRA**
Plot 48, Ogwalanjulgu Road, Lira,
Junior Quarter
Tel: +256 414 671032

**WESTER REGION, HOIMA**
Plot 29/31, Main Street Hoima
Tel: +256 465 440688

**SOUTHERN EASTERN REGION, JINJA**
Plot 6 Rippon Garden, Jinja town
Tel: +256 434 122176

**EASTERN REGION, TORORO**
Plot 27 Kwapa Road, Tororo
Tel: +256 454 445195

**SOUTHERN WESTERN REGION, MBARARA**
Mbaguta Estate House 29, Kamukuzi
Mbarara District Local Government Premise
Tel: +256 414 671034

**Follow us on**

www.nda.or.ug
ndauganda.or.ug
Uganda National Drug Authority
+256 791 415565
@UNDAuthority
Ugandanationaldrugauthority